



General

Guideline Title

Edoxaban for treating and for preventing deep vein thrombosis and pulmonary embolism.

Bibliographic Source(s)

National Institute for Health and Care Excellence (NICE). Edoxaban for treating and for preventing deep vein thrombosis and pulmonary embolism. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Aug. 48 p. (Technology appraisal guidance; no. 354).

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

Edoxaban is recommended, within its marketing authorisation, as an option for treating and for preventing recurrent deep vein thrombosis (DVT) and pulmonary embolism (PE) in adults.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

- Deep vein thrombosis (DVT)
- Pulmonary embolism (PE)

Guideline Category

Assessment of Therapeutic Effectiveness
Prevention
Treatment
Clinical Specialty
Cardiology
Emergency Medicine
Family Practice
Geriatrics
Hematology
Internal Medicine
Preventive Medicine
Pulmonary Medicine
Intended Users
Advanced Practice Nurses
Nurses
Physician Assistants
Physicians
Guideline Objective(s)
To assess the clinical effectiveness and cost-effectiveness of edoxaban for treating and preventing deep vein thrombosis (DVT) and pulmonary embolism (PE)
Target Population
Adults aged ≥18 years requiring treatment or secondary prevention of acute deep vein thrombosis (DVT) or pulmonary embolism (PE, with or without DVT)
Interventions and Practices Considered
Edoxaban
Major Outcomes Considered

- Clinical effectiveness
 - Mortality
 - Venous thromboembolism (VTE) recurrence
 - Complications of deep vein thrombosis (DVT) or pulmonary embolism (PE) including post thrombotic syndrome (PTS) and chronic thromboembolic pulmonary hypertension (CTEPH)

- Adverse events of treatment (particularly bleeding)
- Health-related quality of life
- Cost-effectiveness

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Care Excellence (NICE) commissioned an independent academic centre to perform an assessment of the manufacturer's submission on the technology considered in this appraisal and prepare an Evidence Review Group (ERG) report. The ERG report for this technology appraisal was prepared by BMJ Technology Assessment Group (BMJ–TAG) (see the "Availability of Companion Documents" field).

Clinical Effectiveness

Description and Critique of Company's Search Strategy

The company provided two search strategies in the company's submission (CS) for the review of clinical effectiveness, one for head to head randomised controlled trials (RCTs) which is also the source of trials for a network meta-analysis (NMA). The second search strategy is designed to identify non-RCTs.

In the CS it is reported that the following databases were searched:

- MEDLINE and MEDLINE In-Process (using OVID platform)
- EMBASE (using OVID Platform)
- The Cochrane Library, including the following:
 - The Cochrane Database of Systematic Reviews
 - The Cochrane Central Register of Controlled Trials
 - Database of Abstracts of Reviews of Effectiveness

The company reported that the initial search of electronic databases was conducted from inception until May 2014 and updated on 1st December 2014.

The company used a combination of free-text search terms and Medical Subject Heading (MESH) terms covering the following:

- Population of interest: adults ≥18 years old requiring treatment or secondary prevention of deep vein thrombosis (DVT) and pulmonary embolism (PE)
- Interventions of interest: edoxaban, dabigatran, rivaroxaban, warfarin, or vitamin K antagonists
- Study types: RCTs and non-randomised studies
- Exclusions: case report, letters, historical article, studies were limited to studies in humans

There was no restriction based on language applied in the database search strategies used by the company. The ERG considers the company to have conducted comprehensive searches using a variety of different electronic medical databases. In addition, the company reports scrutinising bibliographic reference lists of included studies and systematic reviews reports for relevant studies. The ERG considers the company's approach to searching for relevant studies to be appropriate for the systematic review. The inclusion and exclusion criteria for the systematic review are detailed in Table 3 of the ERG report.

Details of Studies Included in the Review of Clinical Effectiveness

After de-duplication, the company's searches yielded 7216 articles from the search for RCTs for the clinical effectiveness systematic review. Following abstract and full text screening of 181 publications, a total of 2 reports of a single trial (n=1) were included in the review. The included trial was Hokusai-VTE (NCT00986154). The trial was designed to compare edoxaban (60 mg or 30 mg daily) and warfarin (target international normalised ratio [INR] 2.0 to 3.0) for a flexible dosing period of 3 to 12 months.

The ERG notes that no observational studies (non-RCTs) were identified for inclusion from the company's searches for the systematic review of clinical effectiveness. The ERG is not aware of any additional primary studies potentially relevant to this single technology appraisal (STA) that have been omitted by the company.

Cost-effectiveness

ERG Comment on Company's Review of Cost-effectiveness Evidence

The following electronic databases were searched: Medline, EMBASE, EconLit, and the Cochrane Library (National Health Service Economic Evaluation Data [NHS EED]). The search was carried out in May 2014 and updated in December 2014. Search terms captured the condition of interest (DVT/PE), a range of interventions (edoxaban, dabigatran, rivaroxaban, apixaban and warfarin) and economic evaluation studies; no limits on the date of publication were applied.

In addition to database searches, bibliographies of systematic reviews articles were examined to obtain additional references and bibliographies of accepted references were also reviewed to identify other potentially relevant references.

A total of 12 cost-effectiveness analyses were identified from the original search (4 studies) and the updated search (8 studies). None of the studies included edoxaban. These considered the cost-effectiveness of apixaban, dabigatran, rivaroxaban or warfarin against at least one comparator. Of the 12 studies, six were performed in the UK; however, none of those six studies have been published in a peer-reviewed journal which potentially reduces their credibility. The company extracted data from these studies and presented these within the submission. The company also undertook a study quality assessment for each of the 12 studies within the appendices.

The ERG considers that the search terms used by the company to identify economic evaluations were comprehensive and appropriate; moreover, the economic filters were comparable to those recommended by Scottish Intercollegiate Guidelines Network (SIGN). However, the ERG notes that searches were not performed in the Health Technology Assessment (HTA) database, which may have resulted in the omission of relevant publications. During clarification the ERG asked the company the rationale for not searching the HTA database. The company's response is presented in Box 18 of the ERG report.

The inclusion and exclusion criteria applied are considered to be reasonable, with the exception of the choice of included interventions. The company restricted included studies to those which evaluated at least one of the following treatments: apixaban, dabigatran, edoxaban, rivaroxaban and warfarin. Economic analyses and cost studies comparing low molecular weight heparin (LMWH), and unfractionated heparin (UFH) that did not evaluate apixaban, dabigatran, edoxaban, rivaroxaban or warfarin were not formally included in the review.

To assess if relevant cost-effectiveness studies were missed during the company's search, the ERG reviewed economic evaluation studies included within the systematic review for three related STAs, TA261 (an STA appraising the use of rivaroxaban for the treatment of acute DVT and secondary prevention of DVT and PE), TA287 (an STA appraising the use of rivaroxaban for the treatment of acute PE and secondary prevention of DVT and PE) and TA327 (an STA appraising the use of dabigatran for the treatment and secondary prevention of DVT and PE). As a consequence of this limit on interventions, the company omitted data from a number of studies which considered only LMWH or UFH, and which were included in TA261 or TA287. However none of these studies were used to inform the economic analysis within TA261 or TA287. In addition, NICE clinical guideline CG144, a guideline relating to the management of venous thromboembolic diseases, was not identified or included.

The ERG considers that cost-effectiveness evidence within these NICE publications are of relevance for this STA; therefore the ERG summarised the data within these studies in Table 23 of the ERG report for completeness.

See Section 5.3 of the ERG report for additional information on cost- effectiveness searches.

Number of Source Documents

Clinical Effectiveness

- Two reports of a single trial (n=1) were included in the review.
- Four additional studies were used for network meta-analysis (NMA).

Cost-effectiveness

- A total of 12 cost-effectiveness analyses were identified from the original search (4 studies) and the updated search (8 studies). None of the studies included edoxaban. Of the 12 studies, six were performed in the UK; however, none of those six studies have been published in a peer-reviewed journal which potentially reduces their credibility.
- The company submitted an economic model.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

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Clinical Effectiveness

Critique of Data Extraction

The company reported that data were extracted from full-text versions of studies or clinical study reports, where available. The company also reported that quality-control procedures for the data extraction included verification of all extracted data with their original sources by a second researcher; "relevant information was abstracted into the single technology appraisal (STA) template into a pre-defined Microsoft Word® document by a reviewer. A second reviewer checked the data extraction and any inconsistencies were resolved through discussion" (company's submission [CS]). The ERG considers contemporaneous, duplicate, data extraction by 2 reviewers, each blind to the judgement of the other, to be the gold standard method of data extraction. The ERG notes the company reports items from the Consolidated Standards of Reporting Trials (CONSORT) statement (2010) within the text of the CS.

Quality Assessment

The company conducted a quality assessment for the trial included in the systematic review of randomised controlled trials (RCTs) using a quality assessment tool that seems to be based on the Cochrane risk of bias tool. A summary of the company's quality assessment for the Hokusai-VTE trial reported within the CS are presented in Table 4 of the ERG report.

The ERG considers the company's approach to quality assessment for the Hokusai-VTE trial to meet with standard practice for the assessment of bias in RCTs and agrees with the quality assessment ratings.

Based on the methods outlined in the CS, the ERG considers that the company followed standard systematic review processes and considers the company's approach to the selection of studies and data extraction for the systematic reviews to be reasonable.

Description and Critique of the Network Meta-analysis

The company conducted network meta-analyses (NMAs) to provide relative treatment effect estimates between different new oral anticoagulants (NOACs) using warfarin as a common comparator regarding efficacy and safety for the treatment and secondary prevention of venous thromboembolism (VTE). The company used a Bayesian Markov Chain Monte Carlo (MCMC) simulation approach to the NMA, using OpenBUGS software to carry out the NMA. The OpenBUGS code used was supplied to the ERG in the company's response to clarification questions. The ERG validated the results generated by the company using the OpenBUGS code supplied for a sample of outcomes.

The inclusion criteria for the NMA are detailed in Table 15 of the ERG report. Studies were included if they met the criteria for the population, comparators and design as well as including at least one of the interventions and outcomes of interest. In addition, only full-text publications were included and there were no language restrictions. Five RCTs are considered in the critique of the NMA.

A summary of the company's quality assessment of these studies is shown in Table 17 of the ERG report.

See Section 4 of the ERG report for more information on clinical effectiveness analysis.

Cost-effectiveness

NICE Reference Case Checklist

Table 24 and Table 25 of the ERG report summarise the ERG's quality assessment of the company's economic evaluation. Table 24 summarises the ERG's appraisal of the company's economic evaluation against the requirements set out in the NICE reference case checklist for the base case analysis, with reference to the NICE scope; Table 25 summarises the ERG's appraisal of the quality of the company's *de novo* economic model using the Philips checklist.

Modelling Approach and Model Structure

The company developed a *de novo* cohort Markov model in Microsoft Excel®. The base case model assumes that patients receive treatment for 12 months, either with warfarin, edoxaban or other NOAC. The company reports that the model captures both the treatment and management of VTE.

All VTE patients enter the model (presented in Figure 7 of the ERG report) in the on treatment state. This health state also portrays the VTE index health state as all patients entering the model have been diagnosed with VTE (acute deep thrombosis [DT], with or without pulmonary embolism [PE], or PE). Whilst on treatment, patients can experience a recurrent VTE event or suffer a treatment-related adverse event like heparin-induced thrombocytopenia (HIT), clinically relevant non-major bleeding (CRNMB) or a major bleed (MB). Patients on treatment can also develop chronic thromboembolic pulmonary hypertension (CTEPH), which can evolve to long-term CTEPH (LT-CTEPH), or experience a stroke. Patients who do not die from a stroke, move on to the post-stroke health state.

Patients experiencing a HIT event, a CRNMB, a MB, CTEPH or a stroke are assumed to stop anticoagulation treatment whilst experiencing the event.

After 12 months of anticoagulation therapy (with edoxaban or any of the comparator drugs), all patients (if alive) move to the off treatment state where they stay for the remaining 49 years of the analysis. During the initial 12 month treatment period patients can also move into the off treatment state if they experience events such as HIT, CRNMB, MB and CTEPH. After moving to the off treatment state at 12 months, patients can still experience recurrent VTE however they do not receive any drug therapy after they move from the recurrent event health state.

Whilst in the on treatment and off treatment states, patients are at risk of developing post-thrombotic syndrome (PTS). Patients can die at any point in the model. Age-dependant mortality was included in the model, along with disease specific mortality. Events such as index VTE, VTE recurrence, MB, CTEPH (long-term or not) and stroke are assumed to be associated with an increased mortality risk.

In their submission the company reports that the probability of VTE recurrence varies with time, with the highest risk of recurrent VTE occurring within the first year after the index event. It is stated that the model takes this into account by using 5 different time periods since the index event. These are the following:

- Day 1 to day 14 1 cycle
- Day 15 to day 98 (3 months) 6 cycles
- Day 99 (4 months) to Day 183 (6 months) 6 cycles
- Day 184 (6 months) to Day 364 (12 months) 13 cycles
- Day 365 (12 months) onwards

Each time period has a corresponding transition matrix in the economic model which is reported to translate different probabilities of events occurring at different points in time after the index VTE event.

See Section 5.4.2.1 of the ERG report for ERG comments on the modelling approach and model structure, and section 5 and 6 of the ERG report for additional information on cost-effectiveness analysis.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Considerations

Technology appraisal recommendations are based on a review of clinical and economic evidence.

Technology Appraisal Process

The National Institute for Health and Care Excellence (NICE) invites 'consultee' and 'commentator' organisations to take part in the appraisal process. Consultee organisations include national groups representing patients and carers, the bodies representing health professionals, and the manufacturers of the technology under review. Consultees are invited to submit evidence during the appraisal and to comment on the appraisal documents.

Commentator organisations include manufacturers of the products with which the technology is being compared, the National Health Service (NHS) Quality Improvement Scotland and research groups working in the area. They can comment on the evidence and other documents but are not asked to submit evidence themselves.

NICE then commissions an independent academic centre to review published evidence on the technology and prepare an 'assessment report'. Consultees and commentators are invited to comment on the report. The assessment report and the comments on it are then drawn together in a document called the evaluation report.

An independent Appraisal Committee then considers the evaluation report. It holds a meeting where it hears direct, spoken evidence from nominated clinical experts, patients and carers. The Committee uses all the evidence to make its first recommendations, in a document called the Appraisal Consultation Document (ACD). NICE sends all the consultees and commentators a copy of this document and posts it on the NICE Web site. Further comments are invited from everyone taking part.

When the Committee meets again it considers any comments submitted on the ACD; then it prepares its final recommendations in a document called the Final Appraisal Determination (FAD). This is submitted to NICE for approval.

Consultees have a chance to appeal against the final recommendations in the FAD. If there are no appeals, the final recommendations become the basis of the guidance that NICE issues.

Who Is on the Appraisal Committee?

NICE technology appraisal recommendations are prepared by an independent committee. This includes health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, its advice is independent of any vested interests.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

Summary of Appraisal Committee's Key Conclusions

Availability and Nature of Evidence

The company developed a new economic model that compared edoxaban with warfarin, rivaroxaban and dabigatran etexilate for the treatment and secondary prevention of an acute venous thromboembolism (VTE) event. The model included 12 states representing treatment status (ontreatment or off-treatment health states), adverse events, and death. The model had a lifetime time horizon (maximum 50 years) and each model cycle was 2 weeks long.

Uncertainties Around and Plausibility of Assumptions and Inputs in the Economic Model

The Committee noted that the modelled clinical-effectiveness estimates were from a network meta-analysis (NMA) which had limited capacity to demonstrate statistically significant differences between treatments. The Committee concluded that there was uncertainty about the cost-effectiveness results.

The Committee noted and agreed with the parameter and structural concerns about the model noted by the Evidence Review Group (ERG), particularly: the assumption that some adverse events were treatment-related rather than disease-related; the exclusion of treatment-switching after VTE recurrence; and the inclusion of both ischaemic and haemorrhagic stroke within the stroke health state. The Committee concluded that some of the assumptions in the model and the model structure lacked clinical plausibility but, taking into account the ERG comments and analyses, these flaws were not key drivers of cost-effectiveness.

The Committee agreed that the cost-effectiveness results were largely driven by the estimates of warfarin monitoring costs, and noted that the costs of monitoring assumed by the company were substantially higher than the range considered plausible in previous appraisals for VTE (£304 to £379). The Committee concluded that the ERG estimates for the first year were closer to those previously accepted as plausible. However, the precise costs of warfarin monitoring remained uncertain.

Incorporation of Health-related Quality-of-Life Benefits and Utility Values. Have Any Potential Significant and Substantial Health-related Benefits Been Identified That Were Not Included in the Economic Model, and How Have They Been Considered?

At entry into the model, for the first cycle only, all patients had a utility value that reflected the disutility of the initial VTE (derived from Hokusai-VTE data). For all subsequent cycles, all patients in all treatment groups were assigned age-dependent baseline utility values from the general population without illness. When patients experienced adverse events in the model, the company applied a health-state-related utility decrement that was deducted from the baseline utility value (derived from its systematic literature review).

Are There Specific Groups of People for Whom the Technology Is Particularly Cost Effective?

The Committee concluded that the trial did not provide relevant data for people with cancer who experienced VTE, and it was unable to make any specific recommendation for this subgroup of patients.

What Are the Key Drivers of Cost-effectiveness?

The Committee agreed that the cost-effectiveness results were largely driven by the estimates of warfarin monitoring costs.

Most Likely Cost-effectiveness Estimate (Given as an ICER)

The Committee agreed that the incremental cost-effectiveness ratio (ICER) was likely to be closer to the ERG estimate of £26,000 per quality-adjusted life year (QALY) gained than the company estimate of approximately £2500 per QALY gained. Nevertheless, it considered that both ICERs were subject to high levels of uncertainty because of parameter and structural uncertainties in the model.

Method of Guideline Validation

External Peer Review

Description of Method of Guideline Validation

Consultee organisations from the following groups were invited to comment on the draft scope, Assessment Report and the Appraisal Consultation Document (ACD) and were provided with the opportunity to appeal against the Final Appraisal Determination.

- Manufacturer/sponsors
- Professional/specialist and patient/carer groups

• Commentator organisations (without the right of appeal)

In addition, individuals selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups were also invited to comment on the ACD.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

The Appraisal Committee considered clinical and cost-effectiveness evidence submitted by the manufacturer of edoxaban and a review of this submission by the Evidence Review Group (ERG). The main clinical effectiveness evidence came from one randomised controlled trial (RCT). For cost-effectiveness, the Appraisal Committee considered an economic model submitted by the manufacturer.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- The Committee noted that there were fewer primary intracranial haemorrhages in the edoxaban group of the trial compared with the warfarin group. It heard from the clinical expert that this was recognised as a benefit of newer oral anticoagulants in general.
- The Appraisal Committee noted that the impact of a deep vein thrombosis (DVT) or pulmonary embolism (PE) can be devastating, with patients often hospitalised, restricted in movement and unable to continue with previous activities. It heard from the patient and clinical experts that the need for international normalised ratio (INR) checks when taking warfarin represents a major disadvantage. The Committee noted that edoxaban has a simple once-daily dosage, and would usually only need 1 annual monitoring visit to check renal function. The Committee concluded that patients value newer oral anticoagulants such as edoxaban, which cause less disruption to their lives than warfarin.

Potential Harms

The summary of product characteristics includes the following adverse reactions for edoxaban: bleeding, anaemia, nausea, rash, hepatobiliary disorders (increased blood bilirubin and gamma-glutamyl transferase) and abnormal liver function test.

For full details of adverse reactions, see the summary of product characteristics.

Contraindications

Contraindications

For full details of contraindications, see the summary of product characteristics.

Qualifying Statements

Qualifying Statements

This guidance represents the views of the National Institute for Health and Care Excellence (NICE) and was arrived at after careful
consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical
judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate

- to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.
- Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

Implementation of the Guideline

Description of Implementation Strategy

 Section 7(6) of the National Institute for Health and Care Excellent 	nce (NICE) (Constitution and Functions) and the Health and Social Care
Information Centre (Functions) Regulations 2013	requires clinical commissioning groups, National Health Services
(NHS) England and, with respect to their public health functions, k	ocal authorities to comply with the recommendations in this appraisal
within 3 months of its date of publication.	
The Welsh Assembly Minister for Health and Social Services has it	issued directions to the NHS in Wales on implementing NICE technology
appraisal guidance. When a NICE technology appraisal recommer	nds the use of a drug or treatment, or other technology, the NHS in Wales
must usually provide funding and resources for it within 3 months o	of the guidance being published.
When NICE recommends a treatment 'as an option', the NHS must	st make sure it is available within the period set out in the paragraphs
above. This means that, if a patient has deep vein thrombosis (DV	T) or pulmonary embolism (PE) and the doctor responsible for their care
thinks that edoxaban is the right treatment, it should be available for	or use, in line with NICE's recommendations.
NICE has developed a costing statement	explaining the resource impact of this guidance.
Implementation Tools	
Mobile Device Resources	
Patient Resources	
Resources	

Institute of Medicine (IOM) National Healthcare Quality Report Categories

For information about availability, see the Availability of Companion Documents and Patient Resources fields below.

IOM Care Need

Getting Better

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Institute for Health and Care Excellence (NICE). Edoxaban for treating and for preventing deep vein thrombosis and pulmonary embolism. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Aug. 48 p. (Technology appraisal guidance; no. 354).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2015 Aug

Guideline Developer(s)

National Institute for Health and Care Excellence (NICE) - National Government Agency [Non-U.S.]

Source(s) of Funding

National Institute for Health and Care Excellence (NICE)

Guideline Committee

Appraisal Committee

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability
Available from the National Institute for Health and Care Excellence (NICE) Web site
Availability of Companion Documents
The following are available:
 Edoxaban for treating and for preventing deep vein thrombosis and pulmonary embolism. Costing statement. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Aug. 1 p. (Technology appraisal guidance; no. 354). Available from the National Institute for Health and Care Excellence (NICE) Web site
Patient Resources
The following is available:
Edoxaban for treating and for preventing deep vein thrombosis and pulmonary embolism. Information for the public. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Aug. 2 p. (Technology appraisal guidance; no. 354). Available from the National Institute for Health and Care Excellence (NICE) Web site Also available for download in ePub and eBook formats from NICE Web site Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients
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NGC Status
This NGC summary was completed by ECRI Institute on November 2, 2015.
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